Amendments to the Specification:

Please replace the paragraph on page 12, lines 21-26, with the following rewritten paragraph:

— As used herein, "wild type" refers to a nucleic acid or polypeptide molecule having the same nucleotide and/or amino acid sequence as a naturally-occurring molecule, respectively. A wildtype hepsin polypeptide molecule has the amino acid sequence of naturally occurring hepsin as shown in Figure 17 **(SEQ ID NO: 8)** or in Leytus et al., (1988 Biochemistry 27:1067-1074), or any fragment or portion thereof. Wildtype hepsin is synthesized as a zymogen, i.e., an enzyme precursor, which is activated upon cleavage of an activation site in its extracellular domain.—

Please replace the paragraphs on page 13, lines 4-14, with the following rewritten paragraphs:

-- As used herein, the term "activation sequence" refers to an amino acid sequence in a molecule which is cleaved by a cognate protease, and which, when cleaved, renders the molecule biologically active e.g. capable of protease activity. In an activated molecule, the activation sequence is cleaved. An example of an activation sequence in the hepsin molecule is RIVGG **(SEQ ID NO: 32)**.

As used herein, the term "substitute activation sequence " refers to an amino acid sequence that replaces an activation sequence found in a wild type molecule. An example of a substitute activation sequence is DDDDK-IVGG **(SEQ ID NO: 3)**, which is substituted for the naturally occurring activation sequence, RIVGG **(SEQ ID NO: 32)**, in hepsin.—

Please replace the paragraph on page 16, lines 26-28, with the following rewritten paragraph:

—Activation of a hepsin molecule can proceed by cleavage of the peptide bond between Arg162-Ile163 in a naturally-occurring activation sequence, R-IVGG (SEQ ID NO: 32), to generate a catalytically active enzyme i.e. an active hepsin.--

Please replace the paragraph on page 17, lines 27-31, with the following rewritten paragraph:

—A full-length, naturally-occurring, human hepsin molecule (Figure 17; SEQ ID NO: 8) (SP Leytus, et al., 1988 Biochemistry 27:1067-1074; K Kurachi, et al., 1994 Methods Enzymol 244:100-114) includes the following: 1) a cytoplasmic domain encompassing amino acid residues 1-17; 2) a transmembrane domain encompassing amino acid residues 18-44; and 3) an extracellular domain encompassing 45-417 and comprising an activation sequence and a catalytic site.--

Please replace the paragraph on page 18, lines 6-12, with the following rewritten paragraph:

-- In one embodiment, a modified hepsin molecule comprises the extracellular domain of a naturally-occurring human hepsin molecule, encompassing amino acid residues 45-417 of the sequence shown in Figure 17 (SEQ ID NO: 8). In another embodiment, a modified hepsin molecule comprises the extracellular domain of a naturally-occurring hepsin molecule modified to include an enterokinase, or other protease recognition sequence, e.g., an enterokinase recognition sequence. Such embodiments are typically soluble molecules because they lack a transmembrane domain (Figure 18; SEQ ID NO: 9).--

Please replace the paragraph on page 24, lines 17-24, with the following rewritten paragraph:

-- The present invention also provides modified hepsin molecules, or fragments or derivative thereof, comprising substitute activation sequences having sequence variations of the substitute activation sequences described above and in Figure 18 (SEQ ID NO: 9). The substitute activation sequence can have conservative amino acid substitutions, where a

substituted amino acid has similar structural or chemical properties. Variants can have non-conservative changes. The variant substitute activation sequences are selected to permit the folded modified hepsin molecule to be cleaved by a cognate protease, thereby generating an activated modified hepsin molecule.--

Please replace the paragraph on page 25, lines 12-17, with the following rewritten paragraph:

-- For example, the amino acid sequence of wild-type, human hepsin (A Torres-Rosado, et al., 1993 Proc Natl Acad Sci USA 90:7181-7185; K Kurachi, et al., 1994 Methods Enzymol 244:100-114) can be used as a basis to predict the distance that spans the activation sequence in a folded human wild type hepsin molecule. The activation sequence of wild-type human hepsin molecule, encompassing residues RIVGG **(SEQ ID NO: 32)**, spans a linear length of five amino acid residues (Figure 17; **SEQ ID NO: 8**).--

Please replace the paragraphs on page 26, lines 12-31, with the following rewritten paragraphs:

-- In one embodiment, an isolated nucleotide sequence encoding a modified hepsin molecule is shown in Figure 9 **(SEQ ID NO: 9)**, beginning at codon agg at position 996 and ending at codon ctc at position 2123. Additionally, the nucleic acid sequence of Figure 9 **(SEQ ID NO: 5)** encodes a signal sequence for protein secretion at position 924-995 and encodes a V5 and 6-His tag sequence at position 2124-2198.

In another embodiment, the isolated hepsin sequence shown in Figure 10 **(SEQ ID NO: 6)** encodes a modified hepsin molecule, beginning with a agg at position 1225 and ending with ctc at position 98. Nucleic acid sequence 1297-1226 of Figure 10 **(SEQ ID NO: 6)** encodes a signal sequence and sequence 97-23 encodes a V5 and 6-His Tag sequence.

The isolated hepsin sequence shown in Figure 11 **(SEQ ID NO: 7)** encodes a modified hepsin molecule, beginning with caa at position 907 and ending with ctc at position 98.

Nucleic acid sequence 979-908 encodes a signal sequence and sequence 97-23 encodes a V5 and 6-His Tag sequence.

A biological sample of the nucleotide sequence shown in Figure 10 **(SEQ ID NO: 6)**, and designated pCEP4W/hepEK was deposited on September 30, 2002, with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 under the provisions of the Budapest Treaty, and has been accorded **an** ATCC **Patent Deposit Designation** ~~accession number~~ (PTA-4733).--

Please replace the paragraphs on page 28, lines 1-34, with the following rewritten paragraphs:

-- molecule sequence, as described in Figures 9-11 **(SEQ ID NOS: 5-7)**. Alternatively, the polynucleotide sequences can be similar to the disclosed sequences.

One embodiment of the invention provides nucleic acid molecules that exhibit sequence identity or similarity with the modified hepsin molecule nucleotide sequences, such as molecules that have at least 60% to 99.9% sequence similarity and up to 100% sequence identity with the sequences of the invention as shown in Figures 9-11 **(SEQ ID NOS: 5-7)**. Another embodiment provides nucleic acid molecules that exhibit between about 75% to 99.9% sequence similarity, and another embodiment provides molecules that have between about 86% to 99.9% sequence similarity. Yet another embodiment provides molecules that have 100% sequence identity with the modified hepsin molecule sequences of the invention as shown in Figures 9-11 **(SEQ ID NOS: 5-7)**.

Complementary Nucleotide Sequences

The present invention also provides nucleic acid molecules that are complementary to the sequences as described in Figures 9-11 **(SEQ ID NOS: 5-7)**, 17-18 **(SEQ ID NOS: 8-9)**. Complementarity can be full or partial. A nucleotide sequence that is fully complementary is complementary to the entire hepsin sequence as described in any one of Figures 9-11 **(SEQ ID NOS: 5-7)** and 17-18 **(SEQ ID NOS: 8-9)**. A nucleotide

sequence that is partially complementary is complementary to only a portion of sequences as described in any one of Figures 9-11 **(SEQ ID NOS: 5-7)** and 17-18 **(SEQ ID NOS: 8-9)**. The complementary molecules include anti-sense nucleic acid molecules. The anti-sense molecules are useful for RNA interference (RNAi), DNA interference, inhibiting growth of a cell or killing a cell expressing a naturally-occurring hepsin molecule or expressing a modified hepsin molecule (A Torres-Rosado, et al., 1993 Proc Natl Acad Sci USA 90:7181-7185). The complementary molecules also include small interfering RNA (siRNA) (Elbashir et al, 2001, Nature 411:494-498; Hammond et al, 2001, Nature Review 2:110-119).

Hybridizing Nucleic Acid Molecules

The present invention further provides nucleic acid molecules having polynucleotide sequences that selectively hybridize to the modified hepsin molecule nucleotide sequence of the invention as shown in any one of Figures 9-11 **(SEQ ID NOS: 5-7)** and 17-18 **(SEQ ID NOS: 8-9)**. The nucleic acid molecules that hybridize can hybridize under high stringency hybridization conditions. Typically, hybridization under standard high stringency conditions will occur between two complementary nucleic acid molecules that differ in sequence complementarity by about 70% to about 100%. It is readily apparent to one skilled in the art that the high stringency hybridization between nucleic acid molecules depends upon, for example, the degree of identity, the stringency of hybridization, and the length of hybridizing strands. The methods and formulas for conducting high stringency hybridizations are well known in the art, and can be found in, for example, Sambrook, et al., in: "Molecular Cloning" (1989).–

Please replace the paragraph on pages 29-30, lines 25-32 and lines1-2, respectively, with the following rewritten paragraph:

--The present invention further provides nucleic acid molecules having fragments of the modified hepsin molecule sequences of the invention, such as a portion of the modified hepsin molecule sequences disclosed herein and as shown in any one of Figures

9-11 (SEQ ID NOS: 5-7) and 18 (SEQ ID NO: 9). The size of the fragment will be determined by its intended use. For example, if the fragment is chosen to encode a modified hepsin molecule comprising the extracellular domain of a naturally-occurring, wild-type hepsin molecule comprising a substitute activation sequence, then the skilled artisan shall select the polynucleotide fragment that is large enough to encode this domain(s). If the fragment is to be used as a nucleic acid probe or PCR primer, then the fragment length is chosen to obtain a relatively small number of false positives during a probing or priming procedure.--

Please replace the paragraph on page 34, lines 1-4, with the following rewritten paragraph:

-- isolated nucleotide sequences that vary from the sequences as described in described in any one of Figures 9-11 (SEQ ID NOS: 5-7) and 17-18 (SEQ ID NOS: 8-9), such that each variant nucleotide sequence encodes a molecule having sequence identity with the amino acid sequence described in Figure 9-11 (SEQ ID NOS: 5-7) and 17-18 (SEQ ID NOS: 8-9).--

Please replace the paragraph on page 39, lines 27-33 and pge 40, lines 1-2, with the following rewritten paragraph:

--The expression vectors can include expression control elements for expression in bacterial host cells. These expression control elements can be induced by environmental conditions such as heat-shock, or by addition of agents such as isopropyl-β-D-thiogalactopyranoside (e.g., IPTG) (N Yamaguchi, et al. 2002 The J of Biol Chem 277:6806-6812). Prokaryotic cell expression vectors are well known in the art and are available from several commercial sources. For example, pGEX vector (Promega, Madison, WI), pTrcHisB vector (Invitrogen), pET vector (e.g., pET-21, Novagen Corp.), the phagemid available from Stratagene ~~BLUESCRIPT~~ (BLUESCRIPT®) ~~phagemid~~ (Stratagene, LaJolla, CA), pSPORT (Gibco BRL, Rockville, MD), or ptrp-lac hybrids can be used to express the modified hepsin molecules in bacterial host cells.--

Please replace the paragraph on page 42, lines 13-28, with the following rewritten paragraph:

-- In bacterial systems, a number of expression vectors can be selected depending upon the use intended for the modified hepsin molecules. For example, when large quantities of the modified hepsin molecules are needed for the induction of antibodies, vectors that direct high level expression of fusion proteins that are soluble and readily purified can be desirable. Such vectors include, but are not limited to, the multifunctional E. coli cloning and expression vectors such as **the phagemid available from Stratagene** (BLUESCRIPT® ~~(Stratagene)~~, in which the modified hepsin molecule nucleotide sequence can be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of galactosidase so that a hybrid protein is produced. Other vectors include the pIN vectors (Van Heeke & Schuster 1989 J Biol Chem 264:5503-5509), and the like. The pGEX vectors (Promega, Madison Wis.) can also be used to express foreign proteins as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems are designed to include heparin, thrombin or factor Xa protease cleavage sites so that the cloned protein of interest can be released from the GST moiety at will. --

Please replace the paragraphs on page 46, lines 1-21, with the following rewritten paragraph:

-- In one embodiment, the antibody of the invention can recognize and bind the modified hepsin molecule comprising an amino acid sequence beginning with arginine position 1 and ending with leucine at position 376 as shown in Figure 18 **(SEQ ID NO: 9)**, or a fragment or derivative thereof.

In another embodiment, the monoclonal antibodies of the invention are those produced by a hybridoma cell line which is designated 14C7, deposited on July 25, 2002, with the

American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 under the provisions of the Budapest Treaty, and accorded an ATCC Patent Deposit Designation ~~accession number~~ (PTA-4561). The monoclonal antibody, 14C7, recognizes and binds the modified hepsin molecule of the invention sequences as described in Figure 18 (SEQ ID NO: 9), starting from arginine at position 1and ending at leucine at position 376, and is an IgG1-kappa isotype.

In another embodiment, the monoclonal antibodies of the invention are those produced by a hybridoma cell line which is designated 94A7, deposited on September 30, 2003, with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 under the provisions of the Budapest Treaty, and accorded an ATCC Patent Deposit Designation ~~accession number~~ (PTA5553). The monoclonal antibody, 94A7, recognizes and binds the hepsin molecule as described in Figure 17 (SEQ ID NO: 8), starting from arginine at position 45 and ending at leucine at position 417, as well as the modified hepsin molecule of the invention sequences as described in Figure 18 (SEQ ID NO: 9), starting from arginine at position 1 and ending at leucine at position 376, and is an IgG2A-kappa isotype. --

Please replace the following paragraph on page 57, lines 20-34 and page 58, lines 1-8, with the following rewritten paragraph:

--Examples of cytotoxic agents include, but are not limited to ricin, ricin A-chain, doxorubicin, daunorubicin, ~~taxol~~ paclitaxel (TAXOL™), ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, epithilones, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, maytansinoids, and glucocorticoid and other chemotherapeutic agents, as well as radioisotopes. Suitable radioisotopes include the following: Antimony-124, Antimony-125, Arsenic-74, Barium-103, Barium-140, Beryllium-7, Bismuth-j206, Bismuth-207, Cadmium-109, Cadmium-115m, Calcium-45, Cerium-139, Cerium-141, Cerium-144, Cesium-137, Chromium-51, Cobalt-56,

Cobalt-57, Cobalt-58, Cobalt-60, Cobalt-64, Erbium-169, Europium-152, Gadolinium-153, Gold-195, Gold-199, Hafnium-175, Hafnium-181, Indium-111, Iodine-123, Iodine-131, Iridium-192, Iron-55, Iron-59, Krypton-85, Lead-210, Lutetium-177, Manganese-54, Mercury-197, Mercury-203, Molybdenum-99, Neodymium-147, Neptunium-237, Nickel-63, Niobium-95, Osmium-185+191, Palladium-103, Platinum-195m, Praseodymium-143, Promethium-147, Protactinium-233, Radium-2226, Rhenium-186, Rubidium-86, Ruthenium-103, Ruthenium-106, Scandium-44, Scandium-46, Selenium-75, Silver-110m, Silver-11, Sodium-22, Strontium-85, Strontium-89, Strontium-90, Sulfur-35, Tantalum-182, Technetium-99m, Tellurium-125, Tellurium-132, Thallium-170, Thallium-204, Thorium-228, Thorium-232, Tin-113, Titanium-44, Tungsten-185, Vanadium-48, Vanadium-49, Ytterbium-169, Yttrium-88, Yttrium-90, Zinc-65, and Zirconium-95. Antibodies can also be conjugated to an anti-cancer pro-drug activating enzyme capable of converting the pro-drug to its active form. –

Please replace the following paragraph on page 58, lines 21-33, and page 59, lines 1-5, with the following rewritten paragraph:

– Radiolabeling of antibodies is accomplished using a chelating agent which is covalently attached to the antibody, with the radionuclide inserted into the chelating agent. Preferred chelating agents are set forth in Srivagtava et al. *Nucl. Med. Bio.* 18:589-603, 1991 and McMurry et al., *J. Med. Chem.* 41:3546-3549, 1998. or derived from the so-called NOTA chelate published in H. Chong, K. et al., *J. Med. Chem.* 45:3458-3464, 2002, all of which are incorporated herein in full by reference. Particularly preferred for conjugation of radioisotopes to ~~an RG1~~ **a hepsin** antibody are derivatives of the bifunctional chelator p-SCN-Benzyl-DPTA (Brechbiel et al., *Inorg. Chem.* 25:2772-2781, 1986); for example, cyclohexyl-DTPA (CHX-A''-DTPA, Wu et al., *Bioorg. Med. Chem.* 10:1925-1934, 1997) and MX-DTPA (1B4M-DTPA, McMurry et al., *J. Med. Chem.*, 41: 3546-3549, 1998), as well as 1,4,7-triazacyclononane-N,N',N''-triacetic acid (NOTA) (Chong et al. *J. Med. Chem.* 45:3458-3464, 2002). Conjugation can be accomplished by the method of Nikula et al. *Nucl. Med. Biol.* 3:387-390, 1995. Particularly preferred for use as a detectable marker for immunoscintigraphy are the radioisotopes ^{111}In or ^{99m}Tc. Preferred detectable markers for positron emitting tomography are ^{43}Sc, ^{44}Sc, ^{52}Fe, ^{55}Co, ^{68}Ga, ^{64}Cu, ^{86}Y and ^{94m}Tc. For immunotherapy,

the beta-emitting radioisotopes ^{46}Sc, ^{47}Sc, ^{48}Sc, ^{72}Ga, ^{73}Ga, ^{90}Y, ^{67}Cu, ^{109}Pd, ^{111}Ag, ^{149}Pm, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{186}Re, and ^{188}Re and the alpha-emitting isotopes ^{211}At, ^{211}Bi, ^{212}Bi, ^{213}Bi and ^{214}Bi, can be used. Preferred are ^{90}Y, ^{177}Lu, ^{72}Ga, ^{153}Sm, ^{67}Cu and ^{212}Bi, and particularly preferred are ^{90}Y and ^{177}Lu.--

Please replace the following paragraph on page 60, lines 10-17, with the following rewritten paragraph:

--The present invention provides crystals and/or molecular structures of the modified hepsin molecules of the invention. Modified hepsin molecules are expressed from the recombinant plasmids described herein e.g., ~~SEQ ID NOs:~~ Figures 9-11 (SEQ ID NOS: 5-7). The expressed protein can be crystallized according to protocols and conditions known to those skilled in the art (A. McPherson, 1999, Crystallization of Biological Macromolecules, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, ISBN: 0879696176; A. Ducruix and R. Giege, 1999, Crystallization of Nucleic acids and Proteins: A Practical Approach, 2nd Edition, Oxford University Press; ISBN: 0199636788).--

Please replace the following paragraph on page 70, lines 23-31, with the following rewritten paragraph:

-- A full-length hepsin probe was generated by RT-PCR amplification. Oligonucleotide primers (sense 5'-AGA GGC AGT GAC ATG GCG CAG AAG GAG GGT-3' (SEQ ID NO: 10) and antisense 5'-TGG AGG CTG CGC AGC GAG AAG-3' (SEQ ID NO: 11)) were designed based on the published human hepsin cDNA sequence (Leytus et al. (1988) *Biochemistry*. 27 (3):1067-74). A cDNA fragment spanning the entire coding region of human hepsin was amplified from total RNA derived from human hepatoma HepG2 cells using a RT-PCR-based method (cDNA Cycle Kit, Invitrogen). PCR products were subcloned into pCR vector (Invitrogen) and sequenced. The cDNA fragment was used as a template for construction of additional plasmid vectors expressing soluble forms of human hepsin.--

Please replace the following paragraph on page 72, lines 11-20, with the following rewritten paragraph:

-- Set 1:

Forward primer	BLX190:1181U21	TCGAGTCCCCATAATCAGCAA (SEQ ID NO: 12)
Reverse primer	BLX190:1253L22	CATCTTGGGCTTGATCTGGTTT (SEQ ID NO: 13)
Probe	BLX190:1204U28	ATGTCTGCAATGGCGCTGACTTCTATGG (SEQ ID NO: 14)

Set 2:

Forward primer	BLX190:643U22	AGGTCATCTCCGTGTGTGATTG (SEQ ID NO: 15)
Reverse primer	BLX190:739L16	CCCACGATGCGGTCCA (SEQ ID NO: 16)
Probe	BLX190:668U21FL	CAGAGGCCGTTTCTTGGCCGC (SEQ ID NO: 17)

PCR amplification was performed under the following conditions: 48°C 30 min; 95°C 10 min; 95°C 15 sec and 60°C 1 min for 40 cycles.--

Please replace the paragraph on page 77, lines 3-10, with the following rewritten paragraph:

-- Oligonucleotide primers (sense 5'-AGA GGC AGT GAC ATG GCG CAG AAG GAG GGT-3' (SEQ ID NO:18))and antisense 5'-TGG AGG CTG CGC AGC GAG AAG-3' (SEQ ID NO: 19))were designed based on the published human hepsin cDNA sequence (Leytus et al. (1988) *Biochemistry*. 27 (3):1067-74). A cDNA fragment spanning the entire coding region of human hepsin was amplified from total RNA derived from human hepatoma HepG2 cells using a RT-PCR-based method (cDNA Cycle Kit, Invitrogen). PCR products were subcloned into pCR vector (Invitrogen) and sequenced. The cDNA fragment was used as a template for construction of additional plasmid vectors expressing soluble forms of human hepsin.--

Please replace the paragraphs on page 77, lines 20-27, with the following rewritten paragraphs:

-- PCR amplification of the V5 and 6His tag from pcDNA 3.1/V5His (Invitrogen, San Diego) was performed using the upstream primer (V5HisFor – 5' CAGCTCGAATTCGGTAAGCCTATCCCT 3' **(SEQ ID NO: 20)**) and the downstream primer (V5HisRev—5' GATGCGGCCGCTTTAAACTCAATGGTG 3'**(SEQ ID NO: 21)**).

PCR amplification of hepsin was performed using the upstream primer (NXhpsnfor-- 5' CATATGCCCGGGAGGAGTGACCAGGAG 3'**(SEQ ID NO: 22)**), the downstream primer (hpsnrev—5' CTTACCGAATTCGAGCTGGGTCACCAT 3'**(SEQ ID NO: 23)**).--

Please replace the paragraphs on page 78, lines 27-33, and page 79, lines 1- 16, with the following rewritten paragraphs:

-- The plasmid construct pIRESpuro2W/hepEK having a hepsin insert was generated in order to express hepsin ED/EK in CHO cells (Figure 9 **(SEQ ID NO: 5)**). (ED=ectodomain=extracellular domain; EK=enterokinase cleavage site)

The cDNA encoding soluble hepsin ED/EK was amplified as a PCR product with the primer pair of hepBspE1_F (CTGATCCGGAcAGGAGTGACCAGGAGCCGC **(SEQ ID NO: 24)**) and hep_R2 (GCCGGGTC CCAGGAAAGGA **(SEQ ID NO: 25)**). pAcGP67/hepED/EK, described supra, served as template. The PCR product was digested with BspEI + NotI for cloning into the expression vector pIRESpuro2W described infra. This PCR fragment includes hepsin ED/EK and two tags: V5 and 6-His.

An Igκ signal sequence was PCR amplified from pSecTag2A (Invitrogen) using the following primers: IgκF (gatcgatatcgccaccatggagacagacacactcctgctat gggtactgctgctctgggttccagg **(SEQ ID NO: 26)**) and IgκR

(atcgTCCGGAGCGTCACCAGTGGAACCT GGAACCCAGAGCAGCAGt (SEQ ID NO: 27)). EcoRV and BspEI were used to create compatible ends for ligation.

pIRESpuro2W (a derivative of pIRESpuro2 that was originally purchased from ClonTech, modified in house) was linearized with EcoRV/NotI and used as vector backbone.

pIRESpuro2W/hepEK (Figure 9 (SEQ ID NO: 5) was constructed by three-way ligation (Fast-Link DNA ligation kit, Epicentre) of the restricted PCR fragments described above (Igκ signal sequence, hepsin ED/DK) into pIRESpuro2W.--

Please replace the paragraph on page 79, lines 24-34 and page 80, lines 1-2, with the following rewritten paragraph:

-- The KpnI—hepEK--NotI fragment from pIRESpuro2W/hepEK was cloned into the KpnI/NotI site of pCEP4W to create pCEP4W/hepEK (Figure 10 (SEQ ID NO: 6)) for transient expression of hepsin ED/EK in 293EBNA cells (Edge Biosystems).

Plasmid pCEP4W/hepEK36 (i.e., pCEP4W/hep36)

A cDNA fragment encoding the serine protease domain of soluble hepsin ED/EK(hep36) was PCR amplified from pAcGP67/hepsin ED/EK using primers hep36_F (GAGATCCGGACCAAG ACTGTGGCCGTAGGAAGCTG (SEQ ID NO: 28)) and hep36_R (GCCGGGTCCCAGGAA AGGA (SEQ ID NO: 29)). The hepsin ED/EK fragment (from BspEI to NotI) in pCEP4W/hepEK was replaced by the PCR product of hep36 to create the construct pCEP4W/hepEK36 (Figure 11 (SEQ ID NO: 7)).--

Please replace the following paragraph on page 80, lines 9-11, with the following rewritten paragraph:

-- Primers were synthesized that place flanking KpnI sites on the Hepsin ectodomain: srfhepfor2 (5' TGCAGGTACCTAGGAGTGACCAGGAGCCGCTG 3'

(SEQ ID NO: 30)); srfheprev2 (5' CCGGGGTACCAGCTGGGTCACCATGCCGCTGGC 3' (SEQ ID NO: 31)).—